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Finally, plague is plague

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Within 1 month, an international research team published twin papers reporting recovery of the complete genome sequence of *Yersinia pestis* in skeletons buried during the 1348 epidemics in London [1,2]. The first paper reported on the *psp1* plasmid sequence, [1] and the second paper reported on the chromosome and the two other *Y. pestis* plasmid sequences [2]. These data leave no doubt that these individuals died of plague, and they add one more flag to the European map of documented plague sites. Thirteen years ago, the sequence-based, clear-cut molecular detection of *Y. pestis* in individuals buried during a 1722 Marseilles plague epidemic [3,4] had been published, and recent twin papers confirmed and extended our previous discovery.

The Black Death was not only deadly but also mistifying, as the complete medieval *Y. pestis* genome sequence was recovered in the very same place where a previous investigation conducted by some co-authors of the recent twin papers led to the conclusion that plague was absent in 14th-century London [5]. The present study therefore ends a 13-year-period when some scientists and other investigators relied on a sole, flawed negative publication to proclaim, in spite of cumulative evidence published by different research teams using both DNA-based and antigen-based techniques, baseless hypotheses regarding the aetiology of the two historical plague epidemics in Europe.

These twin studies analysed the total DNA extracted from the dental pulp collected from the skeletons, an approach promoted in 1998 [3,4], and that has been further successfully applied to the retrieval of several pathogens in ancient individuals, such as *Mycobacterium tuberculosis* and *Mycobacterium leprae* [6], the louse-borne pathogens *Rickettsia prowazekii* and *Bartonella quintana* [7–10], and *Salmonella enterica* Typhi as the aetiological agent of the so-called Athens plague [11]. There are several biotypes of modern *Y. pestis* organisms, characterised by unique biochemical profiles, and it had been hypothesized, without any evidence, that the Antiqua biotype was responsible for the first historical plague pandemic, and the Medievalis biotype for the Black Death [12]. The analysis of the complete medieval *Y. pestis* strain genome clearly indicated it was not of the Medievalis biotype, refuting this unproved hypothesis. Previous evidences showed that medieval plague was not caused by a Medievalis biotype strain, and that Justinian plague was not caused by an Antiqua biotype strain [13,14]. This point warrants further analysis: knowing which *Y. pestis* biotype(s) has the capacity to promote huge, deadly epidemics matters in the current situation of several thousands of new plague cases reported every year to the WHO.

Somewhat disappointing was the observation that the medieval *Y. pestis* complete genome lacked any unique virulence trait that might have explained the unique epidemiological features of the Black Death, an epidemic that reportedly killed one-third of the European medieval population, that extended to the north of Europe, and occurred in the absence of the known rat reservoir [15]. Therefore, the co-authors of the twin papers advocate several environmental factors that may have contributed to these unique epidemiological traits. In fact, it was proposed that Black Death did not result from any specific virulence trait in the medieval *Y. pestis* strain, but rather from the adaptation of this *Y. pestis* strain to an additional vector, most likely the human louse [16]. Detailed investigation of its genome sequence may reveal specific genetic traits that are related to such adaptation.

Finally, these twin papers close a period of confusion based on a single flawed paper regarding the aetiology of Black Death; 13 years later, it has been finally proven that medieval plague was plague.

Transparency Declaration

No conflict of interest to be declared.

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